```
===============================================================
Sequence Listing could not be accepted due to errors.
See attached Validation Report.
If you need help call the Patent Electronic Business Center at (866)
217-9197 (toll free).
Reviewer: Anne Corrigan
Timestamp: [year=2009; month=4; day=25; hr=19; min=14; sec=39; ms=583; ]
===============================================================
```

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*************************************************************
Reviewer Comments:
<120> Device a method for detecting low density lipoprotein receptor
gene mutations associated with familial hypercholesterolemia

The above <120> response exceeds the Sequence Rules' required 72-
character line limit; please adjust the line.

<210> SEQ 1

Please remove the "SEQ" in the above <210> response; just show <210> 1.
This error appears in subsequent sequences.

(from Sequence 1)
atatggtatt tattatgcac cgagtgtggc tctaatcact tttttttttt taattgagag 10920
acagcctggc tctgttgatt gggctggagt gcagtggcgc gaccgtagct cattgcagcc 10980


Please show only one space between groups of nucleotides.

actgcctggc agaggctgcg agc atg ggg ccc tgg ggc tgg aaa ttg cgc  15350
            met gly pro trp gly trp lys leu arg
            -21 -20             -15
tgg acc gtc gcc ttg ctc ctc gcc gcg gcg ggg act gca g gtaaggcttg 15400
trp thr val ala leu leu leu ala ala ala gly thr ala v
        -10                -5              -1  1


Please show the initial letters of the above amino acids in upper-case
letters (e.g., Met Gly). Please show all codons as three letters with a
space between each codon.
```

```
<210> SEQ 2
<211> 24
<212> DNA
<213> Artificial  sequence
<220>
<221> oligonucleotide
<223> Ex1F
```

Remove "SEQ" from the above <210> line; also, move "oligonucleotide" to the <223> line. Same error in subsequent sequences.
****

Application No: 10542937   Version No: 2.0

Input Set:

Output Set:

Started: 2009-04-15 14:29:52.963
Finished: 2009-04-15 14:30:12.857
Elapsed: 0 hr(s) 0 min(s) 19 sec(s) 894 ms
Total Warnings: 341
Total Errors: 2028
No. of SeqIDs Defined: 259
Actual SeqID Count: 238

Error code	Error Description
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 259	Found undefined lettercode; POS (281) SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 300, Calculated : 301 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 360, Calculated : 361 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 420, Calculated : 421 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 480, Calculated : 481 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 540, Calculated : 541 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 600, Calculated : 601 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 660, Calculated : 661 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 720, Calculated : 721 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 780, Calculated : 781 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 840, Calculated : 841 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 900, Calculated : 901 SEQID(0)
E 254	The total number of bases conflicts with running total, Input:

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                      Input Set:


                      Output Set:



              Started:  2009-04-15 14:29:52.963
             Finished:  2009-04-15 14:30:12.857
              Elapsed:  0 hr(s) 0 min(s) 19 sec(s) 894 ms
       Total Warnings:  341
         Total Errors:  2028
  No. of SeqIDs Defined: 259
    Actual SeqID Count:  238
```

Error code	Error Description
	961 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 1020, Calculated : 1021 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 1080, Calculated : 1081 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 1140, Calculated : 1141 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 1200, Calculated : 1201 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 1260, Calculated : 1261 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 1320, Calculated : 1321 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 1380, Calculated : 1381 SEQID(0)
E 254	The total number of bases conflicts with running total, Input: 1440, Calculated : 1441 SEQID(0) This error has occured more than 20 times, will not be displayed
E 259	Found undefined lettercode; POS (8762) SEQID(0)
E 259	Found undefined lettercode; POS (8773) SEQID(0)
E 259	Found undefined lettercode; POS (8794) SEQID(0)
E 259	Found undefined lettercode; POS (8805) SEQID(0)
E 259	Found undefined lettercode; POS (8816) SEQID(0)
E 259	Found undefined lettercode; POS (8827) SEQID(0)
E 259	Found undefined lettercode; POS (8838) SEQID(0)
E 259	Found undefined lettercode; POS (8849) SEQID(0)
E 259	Found undefined lettercode; POS (8860) SEQID(0)

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            Input Set:


            Output Set:



         Started:    2009-04-15 14:29:52.963
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  Total Warnings:    341
    Total Errors:    2028
No. of SeqIDs Defined:    259
 Actual SeqID Count:    238


Error code      Error Description


E  259      Found undefined lettercode; POS (8871) SEQID(0)

W  333         tabs used in amino acid numbering  SEQID (0)

W  333         tabs used in amino acid numbering  SEQID (0)

W  333         tabs used in amino acid numbering  SEQID (0)

E  342         'n' position not defined  found at POS:  26149 SEQID(0)

E  342         'n' position not defined  found at POS:  26158 SEQID(0)

E  342         'n' position not defined  found at POS:  26164 SEQID(0)

W  333         tabs used in amino acid numbering  SEQID (0)

E  342         'n' position not defined  found at POS:  26266 SEQID(0)

E  342         'n' position not defined  found at POS:  26287 SEQID(0)

W  333         tabs used in amino acid numbering  SEQID (0)

E  323         Invalid/missing amino acid numbering  SEQID (0)  POS (1)

E  342         'n' position not defined  found at POS:  28723 SEQID(0)

W  333         tabs used in amino acid numbering  SEQID (0)

E  342         'n' position not defined  found at POS:  28786 SEQID(0)

E  342         'n' position not defined  found at POS:  28807 SEQID(0)

W  333         tabs used in amino acid numbering  SEQID (0)

E  342         'n' position not defined  found at POS:  28867 SEQID(0)

E  342         'n' position not defined  found at POS:  28882 SEQID(0)

W  333         tabs used in amino acid numbering  SEQID (0)

E  342         'n' position not defined  found at POS:  31357 SEQID(0)

W  333         tabs used in amino acid numbering  SEQID (0)
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              Input Set:


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                  Started:   2009-04-15 14:29:52.963
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                  Elapsed:   0 hr(s) 0 min(s) 19 sec(s) 894 ms
          Total Warnings:    341
            Total Errors:    2028
    No. of SeqIDs Defined:   259
      Actual SeqID Count:    238


Error code      Error Description


E   342     'n' position not defined  found at POS:  31443 SEQID(0)

W   333     tabs used in amino acid numbering  SEQID (0)

E   323     Invalid/missing amino acid numbering  SEQID (0)  POS (4)

E   323     Invalid/missing amino acid numbering SEQID (0)at Protein (5)

E   323     Invalid/missing amino acid numbering  SEQID (0)  POS (9)

E   323     Invalid/missing amino acid numbering SEQID (0)at Protein (10)

E   323     Invalid/missing amino acid numbering  SEQID (0)  POS (14)

E   323     Invalid/missing amino acid numbering SEQID (0)at Protein (15)

E   342     'n' position not defined  found at POS:  31626 SEQID(0)

E   342     'n' position not defined  found at POS:  31632 SEQID(0)

E   342     'n' position not defined  found at POS:  31653 SEQID(0)

E   323     Invalid/missing amino acid numbering  SEQID (0)  POS (3)

E   323     Invalid/missing amino acid numbering SEQID (0)at Protein (5)

E   323     Invalid/missing amino acid numbering  SEQID (0)  POS (8)

E   323     Invalid/missing amino acid numbering SEQID (0)at Protein (10)

E   323     Invalid/missing amino acid numbering  SEQID (0)  POS (13)

E   323     Invalid/missing amino acid numbering SEQID (0)at Protein (15)

E   342     'n' position not defined  found at POS:  31719 SEQID(0)

E   323     Invalid/missing amino acid numbering  SEQID (0)  POS (2)

E   323     Invalid/missing amino acid numbering SEQID (0)at Protein (5)

E   323     Invalid/missing amino acid numbering  SEQID (0)  POS (7)

E   323     Invalid/missing amino acid numbering SEQID (0)at Protein (10)
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Started:	2009-04-15 14:29:52.963
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No. of SeqIDs Defined:	259
Actual SeqID Count:	238

Error code	Error Description
E 323	Invalid/missing amino acid numbering SEQID (0) POS (12)
E 323	Invalid/missing amino acid numbering SEQID (0)at Protein (15)
E 342	'n' position not defined found at POS: 31806 SEQID(0)
E 342	'n' position not defined found at POS: 31833 SEQID(0)
E 323	Invalid/missing amino acid numbering SEQID (0) POS (1) This error has occured more than 20 times, will not be displayed
E 342	'n' position not defined found at POS: 32096 SEQID(0)
E 342	'n' position not defined found at POS: 33124 SEQID(0) This error has occured more than 20 times, will not be displayed
W 333	tabs used in amino acid numbering SEQID (0)
W 333	tabs used in amino acid numbering SEQID (0)
W 333	tabs used in amino acid numbering SEQID (0)
W 333	tabs used in amino acid numbering SEQID (0)
W 333	tabs used in amino acid numbering SEQID (0)
W 333	tabs used in amino acid numbering SEQID (0)
W 333	tabs used in amino acid numbering SEQID (0)
W 333	tabs used in amino acid numbering SEQID (0)
W 333	tabs used in amino acid numbering SEQID (0)
E 253	The number of bases differs from <211> Input: 60000 Calculated:62488 SEQID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID

```
                 Input Set:


                 Output Set:



              Started:   2009-04-15 14:29:52.963
             Finished:   2009-04-15 14:30:12.857
              Elapsed:   0 hr(s) 0 min(s) 19 sec(s) 894 ms
      Total Warnings:    341
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 No. of SeqIDs Defined:  259
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Error code	Error Description
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
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E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)

Input Set:

Output Set:

Started:	2009-04-15 14:29:52.963
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Elapsed:	0 hr(s) 0 min(s) 19 sec(s) 894 ms
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Total Errors:	2028
No. of SeqIDs Defined:	259
Actual SeqID Count:	238

Error code	Error Description
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)

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              Input Set:


              Output Set:



                 Started:  2009-04-15 14:29:52.963
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     No. of SeqIDs Defined:  259
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Error code	Error Description
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID
W 402	Undefined organism found in <213> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 202	Invalid input format; Value must be an integerin <210> in SEQID (0)
W 402	Undefined organism found in <213> in SEQ ID (0) This error has occured more than 20 times, will not be displayed
E 257	Invalid sequence data feature in <221> in SEQ ID (0)
E 257	Invalid sequence data feature in <221> in SEQ ID (0) This error has occured more than 20 times, will not be displayed
E 253	The number of bases differs from <211> Input: 20 Calculated:19
E 259	Found undefined lettercode; POS (22) SEQID(0)
E 259	Found undefined lettercode; POS (23) SEQID(0)
E 259	Found undefined lettercode; POS (24) SEQID(0)
E 259	Found undefined lettercode; POS (25) SEQID(0)
W 112	Upper case found in data; Found at position(25) SeqId(0)
W 112	Upper case found in data; Found at position(26) SeqId(0)
W 112	Upper case found in data; Found at position(27) SeqId(0)
E 253	The number of bases differs from <211> Input: 21 Calculated:28
E 259	Found undefined lettercode; POS (21) SEQID(0)
E 259	Found undefined lettercode; POS (22) SEQID(0)

```
        Input Set:


        Output Set:



            Started:   2009-04-15 14:29:52.963
           Finished:   2009-04-15 14:30:12.857
            Elapsed:   0 hr(s) 0 min(s) 19 sec(s) 894 ms
     Total Warnings:   341
       Total Errors:   2028
 No. of SeqIDs Defined:  259
   Actual SeqID Count:   238
```

Error code	Error Description
E 259	Found undefined lettercode; POS (23) SEQID(0)
E 259	Found undefined lettercode; POS (24) SEQID(0)
W 112	Upper case found in data; Found at position(24) SeqId(0)
W 112	Upper case found in data; Found at position(25) SeqId(0)
W 112	Upper case found in data; Found at position(26) SeqId(0)
E 253	The number of bases differs from <211> Input: 20 Calculated:27
E 259	Found undefined lettercode; POS (21) SEQID(0) This error has occured more than 20 times, will not be displayed
W 112	Upper case found in data; Found at position(24) SeqId(0)
W 112	Upper case found in data; Found at position(25) SeqId(0)
W 112	Upper case found in data; Found at position(26) SeqId(0)
E 253	The number of bases differs from <211> Input: 20 Calculated:27
W 112	Upper case found in data; Found at position(24) SeqId(0)
W 112	Upper case found in data; Found at position(25) SeqId(0)
W 112	Upper case found in data; Found at position(26) SeqId(0)
E 253	The number of bases differs from <211> Input: 20 Calculated:27
W 112	Upper case found in data; Found at position(24) SeqId(0)
W 112	Upper case found in data; Found at position(25) SeqId(0)
W 112	Upper case found in data; Found at position(26) SeqId(0)
E 253	The number of bases differs from <211> Input: 20 Calculated:27
W 112	Upper case found in data; Found at position(24) SeqId(0)
W 112	Upper case found in data; Found at position(25) SeqId(0)
W 112	Upper case found in data; Found at position(26) SeqId(0)

```
            Input Set:


            Output Set:



             Started:   2009-04-15 14:29:52.963
            Finished:   2009-04-15 14:30:12.857
             Elapsed:   0 hr(s) 0 min(s) 19 sec(s) 894 ms
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        Total Errors:   2028
 No. of SeqIDs Defined: 259
   Actual SeqID Count:  238
```

Error code	Error Description
E 253	The number of bases differs from <211> Input: 20 Calculated:27
W 112	Upper case found in data; Found at position(27) SeqId(0)
W 112	Upper case found in data; Found at position(28) SeqId(0) This error has occured more than 20 times, will not be displayed
E 253	The number of bases differs from <211> Input: 23 Calculated:30
E 253	The number of bases differs from <211> Input: 23 Calculated:30
E 253	The number of bases differs from <211> Input: 19 Calculated:26
E 253	The number of bases differs from <211> Input: 23 Calculated:30
E 253	The number of bases differs from <211> Input: 23 Calculated:30
E 253	The number of bases differs from <211> Input: 21 Calculated:28
E 253	The number of bases differs from <211> Input: 21 Calculated:28
E 253	The number of bases differs from <211> Input: 23 Calculated:30
E 253	The number of bases differs from <211> Input: 23 Calculated:30
E 253	The number of bases differs from <211> Input: 21 Calculated:28
E 253	The number of bases differs from <211> Input: 21 Calculated:28
E 253	The number of bases differs from <211> Input: 21 Calculated:28 SEQID (0)
E 252	Calc# of Seq. differs from actual; 259 seqIds defined; count=238
E 250	Structural Validation Error; Sequence listing may not be indexable

SEQUENCE LISTING

<110>   Mata Lopez, Pedro
        Mozas Alonso, Pilar
        Pocovi Mieras, Miguel
        Tejedor Hernandez, Diego
        Mallen Perez, Miguel
        Alonso Karlezi, Alberto
        Reyes Leal, Gilbert
        Castillo Fernandez, Sergio
        Martinez Martinez, Antonio
<120> Device a method for detecting low density lipoprotein receptor gene mutations associated
with familial hypercholesterolemia
<130> U 015859-4
<140> 10/542,937
<141> 2006-09-08
<160> 259

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